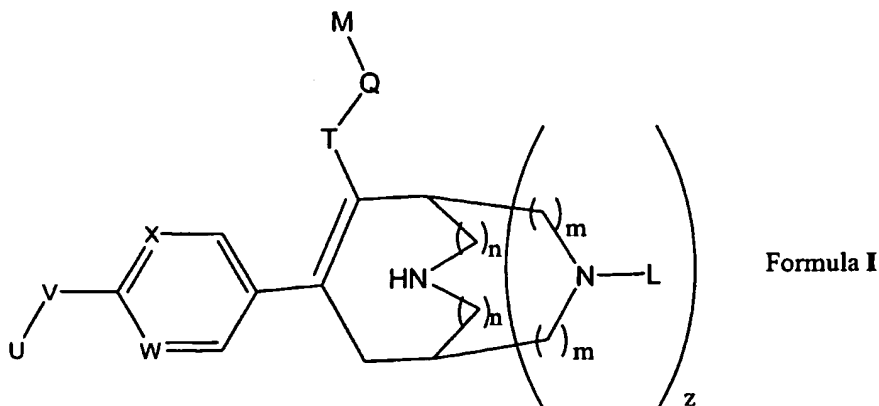


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Claims

1. Compounds of the general formula I



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wherein

X and W represent independently a nitrogen atom or a -CH- group;

V represents $-(CH_2)_r-$; $-A-(CH_2)_s-$; $-CH_2-A-(CH_2)_t-$; $-(CH_2)_s-A-$; $-(CH_2)_2-A-(CH_2)_u-$; $-A-(CH_2)_v-B-$; $-CH_2-CH_2-CH_2-A-CH_2-$; $-A-CH_2-CH_2-B-CH_2-$; $-CH_2-A-CH_2-CH_2-B-$; $-CH_2-CH_2-CH_2-A-CH_2-$; $-CH_2-CH_2-CH_2-CH_2-A-CH_2-$; $-A-CH_2-CH_2-B-CH_2-CH_2-$; $-CH_2-A-CH_2-CH_2-B-CH_2-$; $-CH_2-A-CH_2-CH_2-CH_2-B-$; or $-CH_2-CH_2-A-CH_2-CH_2-B-$;

A and B independently represent -O-; -S-; -SO-; -SO₂-;

U represents aryl; heteroaryl;

T represents $-CONR^1-$; $-(CH_2)_pOCO-$; $-(CH_2)_pN(R^1)CO-$; $-(CH_2)_pN(R^1)SO_2-$; or $-COO-$;

Q represents lower alkylene; lower alkenylene;

M represents aryl-O(CH₂)_vR⁵; heteroaryl-O(CH₂)_vR⁵; aryl-O(CH₂)₂O(CH₂)_wR⁵; heteroaryl-(CH₂)₂O(CH₂)_wR⁵;

L represents $-R^3$; $-COR^3$; $-COOR^3$; $-CONR^2R^3$; $-SO_2R^3$; $-SO_2NR^2R^3$;

$-COCH(Aryl)_2$;

R¹ represents hydrogen; lower alkyl; lower alkenyl; lower alkynyl; cycloalkyl; aryl; cycloalkyl - lower alkyl;

R² and R^{2'} independently represent hydrogen; lower alkyl; lower alkenyl; cycloalkyl; cycloalkyl - lower alkyl;

R³ represents hydrogen; lower alkyl; lower alkenyl; cycloalkyl; aryl; heteroaryl; heterocyclyl; cycloalkyl - lower alkyl; aryl - lower alkyl; heteroaryl - lower alkyl;

heterocyclyl - lower alkyl; aryloxy - lower alkyl; heteroaryloxy - lower alkyl, whereby these groups may be unsubstituted or mono-, di- or trisubstituted with hydroxy, $-\text{OCOR}^2$, $-\text{COOR}^2$, lower alkoxy, cyano, $-\text{CONR}^2\text{R}^{2'}$, CO-morpholin-4-yl, CO-((4-loweralkyl)piperazin-1-yl), $-\text{NH}(\text{NH})\text{NH}_2$, $-\text{NR}^4\text{R}^{4'}$ or lower alkyl, with the proviso that
 5 a carbon atom is attached at the most to one heteroatom in case this carbon atom is sp^3 -hybridized;

R^4 and $\text{R}^{4'}$ independently represents hydrogen; lower alkyl; cycloalkyl; cycloalkyl - lower alkyl; hydroxy - lower alkyl; $-\text{COOR}^2$; $-\text{CONH}_2$;

R^5 represents $-\text{OH}$, $-\text{OCOR}^2$, $-\text{COOR}^2$, $-\text{NR}^2\text{R}^{2'}$, $-\text{OCONR}^2\text{R}^{2'}$, $-\text{NCONR}^2\text{R}^{2'}$, cyano, $-\text{CONR}^2\text{R}^{2'}$, SO_3H , $-\text{SONR}^2\text{R}^{2'}$, $-\text{CO-morpholin-4-yl}$, $-\text{CO-((4-loweralkyl)piperazin-1-yl)}$, $-\text{NH}(\text{NH})\text{NH}_2$, $-\text{NR}^4\text{R}^{4'}$, with the proviso that a carbon atom is attached at the most to one
 10 heteroatom in case this carbon atom is sp^3 -hybridized;

m and n represent the integer 0 or 1, with the proviso that in case m represents the integer 1, n is the integer 0, and in case n represents the integer 1, m is the integer 0;

15 p is the integer 1, 2, 3 or 4;

r is the integer 3, 4, 5, or 6;

s is the integer 2, 3, 4, or 5;

t is the integer 1, 2, 3, or 4;

u is the integer 1, 2, or 3;

20 v is the integer 2, 3, or 4;

w is the integer 1 or 2;

z is the integer 0 or 1; if z represents 0, n represents 0;

and optically pure enantiomers, mixtures of enantiomers such as racemates, diastereomers, mixtures of diastereomers, diastereomeric racemates, mixtures of diastereomeric
 25 racemates, and the meso-form; as well as pharmaceutically acceptable salts, solvent complexes and morphological forms.

2. Compounds of general formula I according claim 1 wherein X, W, V, U, T, Q, L, and M are as defined in general formula I and

30 z is 1

n is 0

m is 1.

3. Compounds of general formula I according to any one of claims 1 to 2 wherein X, W, V, U, T, Q, M, m, and n are as defined in general formula I and

z is 1

L represents $-\text{COR}^{3''}$; $-\text{COOR}^{3''}$; $-\text{CONR}^{2''}\text{R}^{3''}$;

- 5 $\text{R}^{2''}$ and $\text{R}^{3''}$ represent independently lower alkyl; lower cycloalkyl - lower alkyl, which lower alkyl and lower cycloalkyl-lower alkyl are unsubstituted or mono-substituted with halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OCOCH}_3$, $-\text{CONH}_2$, $-\text{COOH}$, or $-\text{NH}_2$, with the proviso that a carbon atom is attached at the most to one heteroatom in case this carbon atom is sp^3 -hybridized.

- 10 4. Compounds of general formula I according to any one of claims 1 to 3 wherein X, W, V, U, L, m, n and z are as defined in general formula I and

T represents $-\text{CONR}^1$;

Q represents methylene;

- 15 M represents $\text{aryl-O}(\text{CH}_2)_v\text{R}^5$; $\text{heteroaryl-O}(\text{CH}_2)_v\text{R}^5$; $\text{aryl-O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_w\text{R}^5$; $\text{heteroaryl-}(\text{CH}_2)_2\text{O}(\text{CH}_2)_w\text{R}^5$.

5. Compounds of general formula I according to any one of claims 1 to 4 wherein X, W, U, L, T, Q, M, m, n, and z are as defined in general formula I and

V represents $-\text{CH}_2\text{CH}_2\text{O}-$; $-\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$; $-\text{OCH}_2\text{CH}_2\text{O}-$; $-\text{O-CH}_2\text{-CH}_2-$;

- 20 $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2-$.

6. Compounds of general formula I according to any one of claims 1 to 5 wherein V, U, T, Q, M, L, m, n, and z are as defined in general formula I and

X and W represent a $-\text{CH}-$ group.

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7. Compounds of general formula I according to any one of claims 1 to 6 wherein X, W, V, Q, T, M, L, m, n, and z are as defined in general formula I and

U is a mono-, di-, or trisubstituted phenyl whereby the substituents are halogen; lower alkyl or lower alkoxy.

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8. Compounds of formula I according to any one of claims 1 to 7 wherein

U represents a mono-, di-, or tri- substituted phenyl ring independently substituted with halogen or C1-C4 alkyl;

V represents $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2-$; $-\text{O-CH}_2\text{-CH}_2\text{-O-}$; $-\text{O-CH}_2\text{-CH}_2-$; $-\text{CH}_2\text{-CH}_2\text{-O-}$;

-O-CH₂-CH₂-CH₂-O-; -CH₂-CH₂-CH₂-O-;

X and W represent a -CH- group;

T represents -CONR¹-, wherein R¹ is a cycloalkyl group;

Q represents -CH₂-;

- 5 M represents a substituted pyridyl-O(CH₂)_vR⁵ group substituted with C1-C4 alkyl, wherein R⁵ is hydroxyl; -COOR₂, wherein R² is hydrogen or C1-C4 alkyl; or R⁵ is -CONR²R^{2'}, wherein R² and R^{2'} are hydrogen or C1-C4 alkyl and v is the integer 2 or 3;

L represents hydrogen;

n is the integer 0;

- 10 z is the integer 1; and

m is the integer 1.

9. Compounds of formula I according to any one of claims 1 to 8 wherein

- 15 U represents a tri-substituted phenyl ring substituted independently with halogen or a phenyl ring substituted in 2- and 6- position with chloro and in 4-position with a methyl group;

V represents -O-CH₂-CH₂-CH₂-; -O-CH₂-CH₂-O-;

X and W represent a -CH- group;

T represents -CONR¹-, wherein R¹ is a cyclopropyl group;

- 20 Q represents -CH₂-;

M represents a pyridinyl-O(CH₂)_vR⁵ group, whereby the pyridinyl ring is substituted with a methyl group, wherein R⁵ represents hydroxyl; and v is the integer 2 or 3;

L represents hydrogen;

n is the integer 0;

- 25 z is the integer 1; and

m is the integer 1.

10. The compounds according to any one of claims 1 - 9 selected from the group consisting of

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(rac.)-(1R*, 5S*)-7-{4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-[2-(3-hydroxy-propoxy)-3-methylpyridin-4-ylmethyl]amide;

(*rac.*)-(1*R**, 5*S**)-7-{4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-[2-(3-hydroxy-propoxy)-3-methylpyridin-4-ylmethyl]amide;

(*rac.*)-(1*R**, 5*S**)-7-{4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-[2-(2-hydroxy-ethoxy)-3-methylpyridin-4-ylmethyl]amide;

(*rac.*)-(1*R**, 5*S**)-7-{4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl}-3,9-diazabicyclo[3.3.1]non-6-ene-6-carboxylic acid cyclopropyl-[2-(2-hydroxy-ethoxy)-3-methylpyridin-4-ylmethyl]amide.

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11. Pharmaceutical compositions containing a compound of any one of claims 1 - 10 and usual carrier materials and adjuvants for the treatment or prophylaxis of disorders which are associated with a dysregulation of the renin-angiotensin system (RAS), comprising cardiovascular and renal diseases hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases known to be related to the RAS.

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12. A method for the treatment or prophylaxis of diseases which are related to the RAS comprising hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications, complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases which are related to the RAS, which method comprises administering a compound according to any one of claims 1 to 10 to a human being or animal.

13. The use of compounds according to any one of claims 1 to 10 for the treatment or prophylaxis of diseases which are associated with the RAS comprising hypertension, congestive heart failure, pulmonary hypertension, cardiac insufficiency, renal insufficiency, renal or myocardial ischemia, atherosclerosis, renal failure, erectile dysfunction, glomerulonephritis, renal colic, glaucoma, diabetic complications,

complications after vascular or cardiac surgery, restenosis, complications of treatment with immunosuppressive agents after organ transplantation, and other diseases known to be related to the RAS.

- 5 14. The use of one or more compounds of any one of claims 1 to 8 in combination with other pharmacologically active compounds comprising ACE inhibitors, angiotensin II receptor antagonists, endothelin receptor antagonists, vasodilators, calcium antagonists, potassium activators, diuretics, sympatholitics, beta-adrenergic antagonists, alpha-adrenergic antagonists, for the treatment of disorders as set forth in any one of claims 9 to
- 10 13.